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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/034,451	12/28/2001	Chad A. Mirkin	01-661-A	9317

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1637	15

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n N .	Applicant(s)	
	10/034,451	MIRKIN ET AL.	
	Examin r	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1,2,20-31 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-5,7-16 and 32-34* is/are rejected.

7)☒ Claim(s) *6 and 11-19* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 December 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,10,12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group IV (claims 32-34) in Paper No. 14 is acknowledged. The traversal is on the ground(s) that claims 32-34 require composition of Group II (claims 2 and 5-10), and therefore these two groups should be examined together. This is not found persuasive because claims 32-34 are drawn to a method of detecting a nucleic acid with nanoparticle oligonucleotide conjugates of claim 2, but claim 2 is drawn to nanoparticle-specific binding substance conjugates, therefore nanoparticles of claim 2 cannot be used in the method of claims 32-34. However, claims 32-34 require a composition of Group III (claims 3-19). Therefore, Claims of Groups III (3-19) and IV (32-34) will be examined together.

2. Claims 1, 2, 20-31 and 35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

4. Claims 6-9 and 32-34 do not have the benefit of the filing date of the priority application, 60/293,861, because the following features of the core/shell nanoparticles were not disclosed in the priority application: cores of FePt or FeAu, metal oxide cores, magnetic cores, hybridization using

nanoparticles in the presence of a magnetic field. Therefor a priority date for claims 6-9 and 32-34 is the filing date of the application, 12/28/2001.

Drawings

5. The drawings are objected to under 37 CFR 1.83(a) because they fail to show the difference in the intensity of the spots I-III in Figures 2B and 2C, as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

6. The drawings are objected to because:

A) In Fig. 4 all of the lines have the same thickness, therefore it is not possible to determine which one correspond to 0, 0.3, 0.6 and 0.9 nm shell thickness.

B) In Fig. 5, the photographs are sufficiently dark to obscure the difference between colored and colorless solution.

C) Figure 6 contains reference letters A, B and C, but there are no corresponding letters in the drawing, therefore it is not clear what these letters mean.

A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

7. The disclosure is objected to because of the following informalities: international applications are referenced on pages 6 (lines 6-8), 8 (lines 23, 24) and 9 (lines 3, 4) with a PCT numbers, rather than WO numbers.

Appropriate correction is required.

Claim Objections

8. Claims 11-19 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 11, which is dependent from a product claim 3, is drawn to the steps of making the product of claim 3, therefore it does not further limit claim 3. Claims 11-19 should perhaps be re-written as method claims.

9. Claim 11 is objected to as ending in a semicolon.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 32-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 32 is indefinite over the recitation of "contacting the surface with a solution comprising core/shell nanoparticle oligonucleotide conjugates of claim 2". Claim 2 is drawn to core/shell nanoparticle specific binding substance conjugates, rather than core/shell nanoparticle oligonucleotide conjugates, which are claimed in claim 3.

B) Claim 32 is indefinite, because in step (b) a magnetic field is used to accelerate movement of the nanoparticle conjugate to the surface with bound nucleic acids. However, neither

claim 2 nor claim 3 are drawn to magnetic nanoparticles (not all metals are magnetic), therefore the method would not work.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 3-5, 7 and 10-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Abbott et al. (U. S. Patent No. 6,277,489 B1; cited in the IDS).

Regarding claim 3, 5, 7 and 11-16, Abbott et al. teach a multilayered material comprising a particulate substrate (= core), a metal film layered onto the substrate (= shell) and a recognition moiety attached to the metal layer (col. 4, lines 22-35). The particulate substrate can be any material, such as metal oxide, for example Fe_2O_3, NiO. The particulate substrate may be any metal, selected according to desired properties, for example, being magnetic (col. 9, lines 55-67; col. 10, lines 1-6, 33-67; col. 11, lines 1-4). The particles can be of any size (col. 9, lines 63-65).

The particulate substrate is coated with a metal layer, such as gold, silver, platinum, palladium, nickel and copper, with gold being particularly preferred (col. 9, lines 3-13; col. 11, lines 34-55). An organic layer is attached to the metal layer and provides a link to the recognition moiety.

Regarding claim 4, Abbott et al. teach recognition moieties including biomolecules, such as nucleic acids (col. 12, lines 9-25; col. 16, lines 38-54; col. 19, lines 56-59).

Regarding claim 10, Abbott et al. teach at least one layer of the metal coating (col. 11, lines 44-46).

Note regarding rejection of claims 11-16: these are product-by-process claims, and it is not clear how the method of making a product of claim 3 makes it different from the product of Abbott et al. (see MPEP 2113).

MPEP 2113 Product-by-Process Claims

PRODUCT-BY-PROCESS CLAIMS ARE NOT LIMITED TO THE MANIPULATIONS OF THE RECITED STEPS, ONLY THE STRUCTURE IMPLIED BY THE STEPS.

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) (Claim was directed to a novolac color developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product.).

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abbott as applied to claims 3 and 7 above, and further in view of Mirkin et al. (U.S. Patent No. 6,361,944 B1; cited in the IDS).

A) Claim 8 is drawn to nanoparticle core being magnetic, and claim 9 is drawn to the nanoparticle core comprising Fe_3O_4 or CO_3O_4.

B) The teachings of Abbott et al. are presented above. Abbott et al. do not teach nanoparticle core being magnetic, but they do teach that the metal cores may be selected for their magnetic properties.

C) Mirkin et al. teach nanoparticle-oligonucleotide conjugates used in nucleic acid detection methods (col. 2, lines 6-17). Mirkin et al. teach nanoparticles being magnetic (col. 16, lines 29-32), and Fe_3O_4 core nanoparticles with a silica shell, which can be conjugated to oligonucleotides (col. 33, lines 19-27).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used magnetic-core of Mirkin et al. in the nanoparticles of Abbott et al. The motivation to do so would have been that oligonucleotides attached to magnetic particles could be removed from solution by application of a magnetic field, allowing easy separation of hybridization products from solution.

16. Claims 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abbott et al. (U. S. Patent No. 6,277,489 B1; cited in the IDS) and Mirkin et al. ((U.S. Patent No. 6,361,944 B1; cited in the IDS).

Regarding claim 32, Abbott et al. teach a multilayered material comprising a particulate substrate (= core), a metal film layered onto the substrate (= shell) and a recognition moiety attached to the metal layer (col. 4, lines 22-35). The particulate substrate can be any material, such as metal oxide, for example Fe_2O_3, NiO. The particulate substrate may be any metal, selected according to desired properties, for example, being magnetic (col. 9, lines 55-67; col. 10, lines 1-6, 33-67; col. 11, lines 1-4). The particles can be of any size (col. 9, lines 63-65).

The particulate substrate is coated with a metal layer, such as gold, silver, platinum, palladium, nickel and copper, with gold being particularly preferred (col. 9, lines 3-13; col. 11, lines 34-55). An organic layer is attached to the metal layer and provides a link to the recognition moiety. Recognition moieties include biomolecules, such as nucleic acids (col. 12, lines 9-25; col. 16, lines 38-54; col. 19, lines 56-59).

The multilayered material may be used to capture a molecule in a purification process or an assay, and the captured molecule may be a nucleic acid (col. 24, lines 13-62). The multilayered material may be used to determine the presence or quantity of an analyte in a sample by contacting the sample with a multilayered material, forming a complex between a recognition moiety and an analyte and detecting the analyte (col. 31, lines 44-63).

B) Abbott et al. do not teach nucleic acids bound to a surface or hybridization conducted in the presence of magnetic field using magnetic (Fe_3O_4) core/shell nanoparticles.

C) Regarding claims 32-34, Mirkin et al. teach nanoparticle-oligonucleotide conjugates used in nucleic acid hybridization methods, where the nucleic acid is contacted with nanoparticle-oligonucleotide conjugates under conditions which allow hybridization of the oligonucleotides on nanoparticles with nucleic acids, which results in a detectable change (col. 2, lines 6-17). Mirkin et al. teach analyte nucleic acid bound to a surface (Fig. 13A).

Mirkin et al. teach nanoparticles being magnetic (col. 16, lines 29-32), and Fe_3O_4 core nanoparticles with a silica shell, which can be conjugated to oligonucleotides (col. 33, lines 19-27). The magnetic nanoparticles can be attached to a satellite probe, which may be labeled with a reporter molecule. The satellite probe is brought in contact with a target, and detection is accomplished by applying a magnetic field, removing particles from solution and measuring the

fluorescence of probe oligonucleotides hybridized to the target (col. 32, lines 44-67; col. 33, lines 1-48; Fig. 24).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have combined magnetic-core particle hybridization of Mirkin et al. with analyte detection assays of Abbott et al. The motivation to do so would have been that oligonucleotides attached to magnetic particles could be removed from solution by application of a magnetic field, allowing easy separation of hybridization products from solution.

17. No references were found teaching or suggesting claims 6 and 11-19. Claims 11-16 are rejected for reasons given above. Claims 17-19 are objected to as being dependent on the rejected claim 11.

18. Claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

June 12, 2003

Teresa Strzelecka, Ph. D.

Patent Examiner

Teresa Strzelecka
6/12/03